*Key Words: social anxiety disorder, paroxetine, treatment*

# Advances in Recognition and Treatment of Social Anxiety Disorder: A 10-Year Retrospective

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***ABSTRACT*** *~ Social anxiety disorder frequently begins in early life and is associated with the subsequent development of comorbid conditions such as depressive and substance use disorders. Social anxiety disorder, particularly the generalized subtype, is characterized by marked impairment in numerous functional domains, including education and social relations. Paroxetine, the first medication to receive an indication in the United States for the treatment of social anxiety disorder, has been shown to be effective in 50% to 60% of patients. The mechanism of action of paroxetine in the treatment of social anxiety disorder is at present unclear. A possible role for early treatment to prevent complications of social anxiety disorder should be explored.* Psychopharmacology Bulletin. *2003;37(Suppl 1): 97–107.*

## INTRODUCTION

Social anxiety disorder (also known as social phobia) is characterized by the fear of being observed or evaluated by others.[1] In social situations, persons with social anxiety disorder fear that they will do or say something to draw negative attention to themselves, and that they will be embarrassed. This fear often results in avoidance of situations in which such scrutiny might take place. In some cases, the individual chooses not to avoid these situations, but instead endures them with intense distress.

## SOCIAL ANXIETY DISORDER AS A DIAGNOSTIC ENTITY

Social anxiety is a nearly universal phenomenon. Almost everyone has had the experience of feeling anxious in situations in which they have been the focus of attention, such as making a speech or giving a classroom presentation. For the vast majority of people, the anxiety is usually not severe enough or not encountered frequently enough to warrant concern. In fact, some degree of social anxiety may actually enhance performance.

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Some individuals, however, experience intense anxiety in situations requiring them to perform in some manner or to interact with others. In such situations, or even in anticipation of them, their anxiety may be so severe that they avoid the situations because the prospect of facing them is too painful. The distress for those stouthearted individuals who do not avoid the feared situation may be intense and, in some cases, disabling. These persons with severe social anxiety and/or avoidance are among a subgroup of the population who suffer from social anxiety disorder. Although experiencing some degree of anxiety in social situations is neither atypical nor pathological, social anxiety disorder is distinguished by the intensity of the anxiety that is experienced and by the accompanying distress or interference in functioning.

Because nearly everyone has experienced social anxiety symptoms at one time or another, there has been a tendency among lay people and professionals alike to trivialize social anxiety disorder. Indifference or lack of knowledge on the part of medical caregivers may pose one of the barriers to care for persons with social anxiety disorder.[2] Persons seeking care for this condition frequently report being told by mental health professionals or other physicians that, "You're just a little bit shy. Don't worry about it…" This is similar to the state of affairs experienced by patients with panic disorder until recently, wherein they were told by physicians "You're just anxious. It's nothing serious. It'll go away." Experienced mental health clinicians, however, realize that conceptualizing social anxiety disorder as "a little bit of shyness" is equally egregious to conceptualizing major depression as "a little bit of sadness". Although social anxiety disorder can, indeed, be mapped on a spectrum of shyness, it is at the extreme end, and well beyond the bound of normality.[3] In fact, although characteristics of shyness overlap substantially with those of social anxiety disorder,[4] the 2 constructs have substantial nonshared variance (eg, it is possible to be extremely shy and yet not meet diagnostic criteria for social anxiety disorder).[5] Still, social anxiety disorder has, until the past decade or so, suffered from a serious lack of research and clinical attention as a consequence of these false assumptions.[6]



### *History of Social Anxiety Disorder as a Diagnostic Entity*

Social phobia did not enter the diagnostic nomenclature of the American Psychiatric Association until the publication of the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition *(DSM-III)*[7]; prior to that, it was generally subsumed within the catch-all phobic neurosis category. According to *DSM-III* criteria, social phobia involved a persistent fear of "a situation in which the individual is exposed to possible scrutiny by others" and is concerned with behaving in a way that will be humiliating or embarrassing. According to this definition, only those

with phobic reactions to a specific phobic situation (such as writing, speaking, or performing in public) could be diagnosed with social phobia. Persons who demonstrated more widespread fear of social situations were, instead, assigned the diagnosis of avoidant personality disorder (APD) on Axis II. In *DSM-III*, APD was first defined as involving hypersensitivity to potential rejection, social withdrawal despite a desire for acceptance, low self-esteem, and reluctance to enter relationships unless given clear assurance of acceptance beforehand.

The *DSM-III* definition of social phobia was criticized as having too narrowly defined the disorder. It was argued that the decision to define social phobia as involving a discrete phobic stimulus and excluding more generalized social fears was not empirically based, nor was it consistent with clinical experience.[6] In the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition-Revised (*DSM-III-R)*, social phobia was more broadly defined to include individuals who had several or many social fears. This necessitated dropping the hierarchical rule excluding a diagnosis of social phobia in the presence of avoidant personality disorder; in *DSM-III-R*, both diagnoses could be made (ie, social phobia on Axis I and APD on Axis II). In recognizing that social phobia can involve fear and avoidance of many social situations, *DSM-III-R* also introduced a provision for denoting a generalized subtype that was defined as involving "most social situations".[8] The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition *(DSM-IV)*[9] did not make substantive changes to the diagnostic criteria for social phobia. It was noted from field trials that concerns about showing signs of anxiety predominated in some individuals, rather than concerns about doing or saying something that could result in humiliation or embarrassment, and therefore, this was added as an alternative diagnostic element (Criterion A). For the first time, explicit mention was made that the diagnosis of social phobia could be applied to children. *DSM-IV* (and the current *DSM-IV,* Text Revision)[1] made mention of the synonym, social anxiety disorder, a term that now appears frequently in the published literature.



### *Subtypes of Social Anxiety Disorder*

Most experts now acknowledge the existence of at least 2 subtypes of social anxiety disorder. The first type, alternatively referred to as discrete, specific, or nongeneralized social anxiety disorder, is the classically described version of social phobia. It is usually confined to a fear of one or a few situations, of which the most common is speaking in front of an audience.[10,11] Although nongeneralized social phobia can most definitely be associated with functional impairment (eg, a student who drops out of college because she cannot speak in front of her seminar group; a salesperson who turns down a promotion because it

will involve speaking at monthly sales meetings), the impairment is usually quite focal.

The second type, referred to as generalized social anxiety disorder, involves fear of a broad array of social situations, typically including both social interactional (eg, speaking to peers over lunch; going to parties; asking a teacher for help) and performance situations (eg, speaking in public; performing in front of an audience).[12-16] From the vantage point of functional impairment, a more or less continuous relationship is seen between the number of social fears and the extent of disability.[17] As such, patients with generalized social anxiety disorder are typically more pervasively affected by their symptoms and their phobic limitations.[18]

## EPIDEMIOLOGY OF SOCIAL ANXIETY DISORDER

### *Social Anxiety Disorder in the General Population*

Up until the mid-1980s, social phobia was thought to be a relatively rare disorder. This belief stemmed from a reliance on clinical psychiatric samples to judge the prevalence of psychiatric disorders, and changed with the advent of community surveys that brought to light the fact that social anxiety disorder is highly prevalent in the general population.



The Epidemiologic Catchment Area (ECA) study found a 2.7% lifetime prevalence of narrowly-defined *DSM-III* social phobia, with a slight predilection for females (2.9%) compared with males (2.5%).[10] This study also highlighted the typically early onset (approximately 50% have onset in childhood) and chronicity of social phobia, and the likelihood that additional comorbid psychiatric disorders (eg, major depression, alcohol/substance abuse) would accrue over time.

More recent studies, using *DSM-III-R* or *DSM-IV* criteria, have found even higher rates of social anxiety disorder. According to the most recent study conducted in the United States, the National Comorbidity Survey (NCS), social anxiety disorder is the third most common psychiatric disorder in the general population—after major depressive and alcohol use disorders—with lifetime, 12-month, and 30-day prevalence rates of 13.3%, 7.9%, and 4.5%, respectively.[19,20] Depending on where one sets the threshold for impairment or distress, rates of social anxiety disorder (like most other psychiatric disorders)[21] will fluctuate.[22] It remains to be seen where the threshold is best set. Even persons with "subthreshold" social anxiety disorder exhibit considerable disability compared with persons without social anxiety symptoms in the community.[17,23] Further research will be required to help inform health policy makers about the optimal cut-off levels for defining which level of social anxiety symptoms would merit intervention. In the absence of such data, we can reasonably use the most conservative estimates to conclude

that social anxiety disorder affects between 2% and 5% of the general adult population.[24] Approximately two thirds of these individuals are thought to suffer from the generalized subtype of the disorder, the subtype that carries the major burden of comorbidity with depressive (and other) disorders.[25,26]

### *Social Anxiety Disorder in Primary Care*

In a study of social anxiety disorder in the general medical healthcare system, investigators found a 1-month prevalence of 4.9% in a French primary care clinic, although there was poor recognition of the disorder on the part of general practitioners and few cases were offered specific treatment of any sort.[27] Katzelnick and colleagues[28] subsequently confirmed and extended these observations in their survey of a large American health maintenance organization, in which they found that virtually none of the patients with social anxiety disorder were being diagnosed or specifically treated. It may be concluded from these data that improved recognition and management of social anxiety disorder in primary care has the potential to enhance outcomes for these patients.[29] Given the high rate of comorbidity with mood disorders in primary care,[30] and the additional functional impairment that can result from this combination of ailments,[31] treatments that can ameliorate both social anxiety and depressive symptoms (eg, selective serotonin reuptake inhibitors [SSRIs]) should be preferred in this setting.



## PAROXETINE TREATMENT OF SOCIAL ANXIETY DISORDER

Although moclobemide, a reversible inhibitor of monoamine oxidase A (RIMA) was shown to be efficacious[32] and received regulatory approval in several countries for the treatment of social phobia in the early to mid-1990s, it failed to distinguish itself from placebo in some other studies[33,34] and is not currently available in the US. The first medication to receive regulatory approval in the US for the treatment of social anxiety disorder was the SSRI, paroxetine. Sertraline and venlafaxine extended-release have also recently received US regulatory Food and Drug Administration (FDA) approval for treatment of this condition. In keeping with the theme of this journal supplement, the focus of the remainder of this article will be on studies of paroxetine for the treatment of social anxiety disorder. Readers interested in reviews of other pharmacotherapeutic and psychotherapeutic options for this condition are referred to recent reviews, consensus statements, and books on these topics.[35-37]

### *Open-Label Study*

One of the first controlled studies to demonstrate the utility of paroxetine for generalized social anxiety disorder was published in the

mid-1990s. In this study, we showed that paroxetine was effective under open-label conditions and, moreover, we provided preliminary indication under double-blind, placebo-controlled conditions that it might prevent relapse.[38] Subsequently, a host of double-blind, placebo-controlled studies demonstrated the unequivocal efficacy of paroxetine for the treatment of social anxiety disorder.

### *Randomized, Controlled Trials*

The first of these was a randomized, controlled trial (RCT) of 187 persons with generalized social anxiety disorder, treated for 12 weeks at 13 centers across the US and 1 in Canada.[39] After a 1-week, single-blind, placebo run-in period, patients received a double-blind, 11-week course of either paroxetine or matching placebo. The initial daily dosage of paroxetine (or placebo) was 20 mg, with weekly flexible increases of 10 mg/d permitted to a maximum dosage of 50 mg/d. The mean dose of paroxetine at study end point was 37 mg (SD, 12 mg); the equivalent mean "dose" of placebo was 45 mg (SD, 18 mg). Fifty (55.0%) of 91 persons taking paroxetine and 22 (23.9%) of 92 persons taking placebo were much improved or very much improved at the end of treatment (odds ratio, 3.88, 95% confidence interval, 2.81-5.36). Mean reduction in Liebowitz Social Anxiety Scale (LSAS)[40] scores from baseline was 30.5 points in the paroxetine group compared with 14.5 points in the placebo group (Figure 1). Improvements in measures of avoidance, fear/anxiety, social life, and work also were significantly greater for paroxetine-treated patients compared with controls.



A study with a very similar design was contemporaneously conducted in 39 centers in Belgium, France, Germany, Ireland, South Africa, Spain, and the United Kingdom.[41] In this study, 290 patients with social anxiety disorder were assigned randomly to 12 weeks of treatment with placebo or paroxetine, also at a flexible dosage of 20-50 mg/d. The proportion of responders was, as in the previously described study,[39] approximately double for subjects receiving paroxetine (65.7%) compared with those receiving placebo (32.4%). The mean reduction in LSAS scores from baseline was 29.4 points in the paroxetine group compared with 15.6 points in the placebo group, again remarkably similar to the results from the previously cited study.

An additional study from Sweden, in which 92 subjects with social anxiety disorder were randomized to receive either paroxetine or placebo, yielded similar results.[42] More recently, results have become available from another large, multicenter study of paroxetine and placebo in the treatment of generalized social anxiety disorder. In this study, 384 patients were randomized to receive a fixed daily dose of paroxetine 20 mg, 40 mg, or 60 mg, or placebo.[43] Response rates were

generally indistinguishable among the 3 different paroxetine doses, which in aggregate outperformed placebo.

Together, these studies provided strong evidence in favor of the utility (and safety) of paroxetine for social anxiety disorder. Based on the latest studies,[43] it is reasonable to conclude that paroxetine 20 mg/d is an effective treatment for many patients with generalized social anxiety disorder, although some patients are likely to benefit from higher dosages.

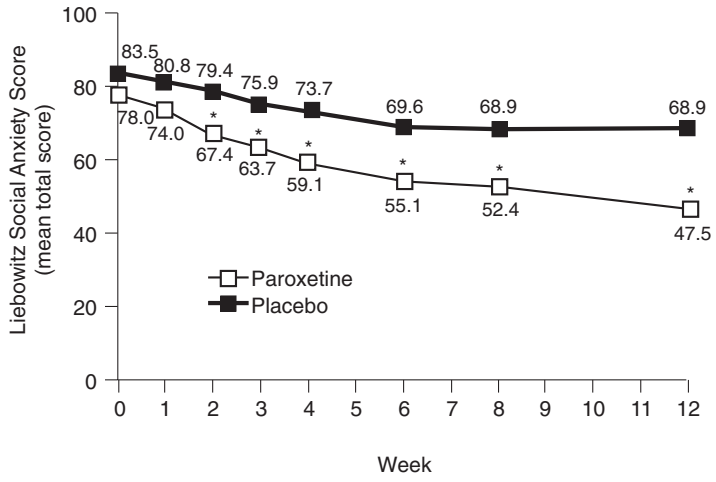
### *Relapse Prevention*

In another study, 437 adults with social anxiety disorder participated in a placebo-controlled, multicenter study comprising a single-blind, acute treatment phase (12 weeks) and a randomized, double-blind, maintenance treatment phase (24 weeks) for patients who had responded to paroxetine during the acute phase. In this study, 323 patients were entered into the maintenance phase, and 257 completed the study (136 paroxetine-treated and 121 placebo-treated patients). Significantly fewer patients relapsed in the paroxetine group than in the placebo group (14% vs 39%; odds ratio, 0.24; 95% confidence interval, 0.14-0.43; $P<.001$). These data substantiate and add to data from shorter-term studies to demonstrate that paroxetine is an effective long-term treatment for social anxiety disorder.[44]



**FIGURE 1**

**12-WEEK MEAN TOTAL LSAS FOR PATIENTS TREATED WITH PAROXETINE VS PLACEBO**




Mean total Liebowitz Social Anxiety Scale (LSAS) for paroxetine- and placebo-treated patients (last observation carried forward) at baseline and by weekly visits through week 12.
*$P<.001$ vs placebo.
Reproduced with permission.[39]

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### *Predictors of Response to Paroxetine*

Overall, the extant data suggest that 50% to 60% of patients with generalized social anxiety disorder are likely to derive clinically meaningful benefit from treatment with paroxetine. In light of this observation, interest has been raised in identifying those persons who are likely to benefit most from treatment and in developing adjunctive treatments to boost response.

Data from 3 placebo-controlled, multicenter trials of paroxetine in social anxiety disorder were pooled to determine predictors of response. Age, gender, duration of illness, symptom severity, or extent of disability at baseline did not predict outcome. Only duration of treatment was a statistically significant predictor of treatment response. Further analysis demonstrated that in paroxetine-treated patients in particular, many nonresponders at week 8 (46/166, or 27.7%) were responders at week 12. These data suggest that a clinical therapeutic trial for social anxiety disorder may need to extend beyond 8 weeks before determining whether it is likely to yield success for any individual patient.[45]



### *Treatment Adjuncts to Paroxetine*

Based both on its β-adrenergic and serotonergic type 1A autoreceptor antagonistic properties, it was hypothesized that pindolol would be effective as an adjunct to paroxetine in the treatment of social anxiety disorder. We conducted a double-blind, placebo-controlled, crossover study comparing addition of 4 weeks of pindolol 5 mg (or placebo) 3 times daily to a steady dose of paroxetine.[46] Subjects were 14 patients with generalized social anxiety disorder who were less than "much improved" following at least 10 weeks of treatment with a maximally tolerated dose of paroxetine. In this study, pindolol was no more effective than placebo in potentiating the effects of paroxetine treatment. Other adjunctive treatments to boost the efficacy of paroxetine (and other SSRIs) should be studied under double-blind conditions.

## FUTURE DIRECTIONS

The neurobiology of social anxiety disorder is poorly understood. It has been hypothesized that abnormalities in brain dopaminergic function underlie the pathophysiology of this disorder.[47,48] Functional neuroimaging studies in social anxiety disorder also have revealed possible alterations in amygdala responsivity.[49] It will be of interest to determine to what extent these abnormalities are remedied as a result of successful treatment with paroxetine (and other efficacious treatment modalities). Preliminary results from a positron emission tomography study in generalized social anxiety disorder suggest that some abnormalities in regional cerebral blood flow are normalized with successful SSRI or

cognitive-behavioral treatment.[50] Observations of this type may help us to understand more about the mechanisms through which paroxetine and other SSRIs exert their therapeutic effects.

Another important avenue for future research will be to test early pharmacological interventions for children with social anxiety. Given the frequent early onset of social anxiety disorder, it has been hypothesized that it may be possible to intervene early with the goal of ameliorating current disability and preventing future complications, such as depressive or substance use disorders.[51,52] The future lies not only in reducing suffering by treating social anxiety disorder once it has manifest, but in detecting it early enough so that optimal functioning can be preserved. Longitudinal research studies in high-risk populations (eg, children showing signs of serious social anxiety and avoidance) will be required to demonstrate the feasibility and effectiveness of such approaches. ✤

## DISCLOSURE

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